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EXAMINER	
EDWARDS, LYDIA E	
ART UNIT	PAPER NUMBER
1797	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/525,538	WIKSWO ET AL.	
	Examiner	Art Unit	
	LYDIA EDWARDS	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25,27-39,42-63 and 65-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25,27-39,42-63 and 65-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

In response to applicant's argument regarding treatment on the merits for any of claims 18, 32 and/or 40, claims 18 and 32 have been treated on the merits. The examiner would like to turn the applicant's attention to page 2 of the office action dated 12/30/2009 where claim 18 was clearly rejected by Kanegasaki. The paragraph heading for the claim rejections contains a typographical error wherein ***claim 19*** was missed typed for that of ***claim 18***. The typographical error does not change the rejection of claim 18 as is what indicated as being rejected in the following paragraph.

As to claim 32, the examiner would like to turn the applicant's attention to pages 6-7 of the office action dated 12/30/2009. The paragraph heading for the claim rejection contains a typographical error wherein ***claims 26-31 and 64-69*** were missed typed for that of ***claim 32***. The typographical error does not change the rejection of claim 32 as the rejection of claim 32 over Kanegasaki (US 20030003571) in view of Lynes (US 20020086280) as applied above to claims 31 and 69, further in view of Henkens et al. (US 6391558) clearly addresses the limitation(s) of only claim 32.

Applicant's arguments with respect to claim 40 have been considered but are moot in view of the cancelation of claim 40.

The objections to claims 40-41 have been withdrawn in view of the cancelations of claims 40-41.

Applicant's arguments with respect to claims 1-7, 9-55 and 57-76 have been considered but are moot in view of the new ground(s) of rejection.

In response to applicant's argument that ***Kanegasaki does not disclose, teach, or suggest a bioreactor having theses features of claim 8, taken alone or in combination with the features recited in amended claim 1,*** applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

In response to applicant's argument that the combination of ***Kanegasaki, Herman and Tuner does not disclose, teach, or suggest a method for culturing a plurality of biofilms as***

recited in amended claim 76, applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

Claim Interpretation - 35 USC § 112

The claim limitations as presented that include "means for" language are being treated under 35 U.S.C. 112, sixth paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 13-18, 20-23, 25, 27-31, 39, 42-44, 48-56, 61, 63, 65-69, 71, and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Hanagan (US 5520787) and Breznak (US 5589352).

Regarding Claims 1-3, 18, 21 23, 27-31 49-51, 56 and 65-69 Kanegasaki discloses a cell motion analysis system comprising a first substrate (Figure 5:7) having first and second surfaces defining a chamber therebetween. A barrier comprising a channel (Figure 5:1) and a plurality of protrusions (Figure 5:6) serve to divide the chamber into a first subchamber (Figure 5:2A) and a second subchamber (Figure 5:2B). This is disclosed in paragraphs [0084], [0085] and [0095]. Paragraph [0097] states that the protrusions and grooves formed within the channels are varied in order to control the diffusion of a particular cell type between the subchambers. Paragraph [0121] states that the gaps of the barrier range from 3 to 50 microns. Figure 12 and paragraph [0112] describe another configuration in which first and second barriers (1) are positioned so as to form a central chamber (2A), an intermediate chamber (2B), and an outer chamber (2C). Furthermore, Kanegasaki teaches that an input port (Figure 3:3Aa) and an input transfer channel are formed in the substrate and provided in fluid communication with the first subchamber. Furthermore, an outlet port (Figure 3:3Ba) and an outlet transfer channel are provided in communication with the second subchamber.

Kanegasaki, however, does not expressly disclose that the apparatus is capable of cultivating living cells, or a means for electrochemical measurements.

Breznak discloses a system similar to that of Kanegasaki in that it is used to measure the chemotactic response of a cell to a chemical. This is described in column 4, line 63 to column 5, line 22 and column 9, line 20 to column 10, line 4. Column 5, lines 22-50 further state that the chemotaxis chamber of Breznak is further adapted to facilitate and monitor cell growth.

Hanagan discloses an apparatus for monitoring cell growth and activity by measuring the concentration of various analytes in the culture solution. Hanagan discloses that a plurality of electrodes (Figure 1:30) are positioned apart from each other so that each electrode is in communication with a flow channel (Figure 1:66) capable of carrying a liquid to be tested. Column 2, lines 8-10 and column 6, lines 35-40 state that the presence of multiple analytes (i.e. glucose and oxygen) are simultaneously detected using different enzymes immobilized on multiple electrodes. The use of counter electrodes, reference electrodes, edge connector pads (Figure 3:350) and electrically conductive leads (Figure 3:360) is disclosed in the abstract and column 8, lines 43-54.

Kanegasaki, Breznak and Hanagan are analogous art because they are from the same field of endeavor regarding cell detection systems.

At the time of the invention, it would have been obvious to ensure that the Kanegasaki chemotaxis apparatus is adapted to additionally facilitate and monitor cell growth. Breznak is evidence that it is well known in the art to encourage and monitor cell growth while simultaneously detecting the cellular response to a chemotactic compound. Hanagan further teaches that cell growth may be detecting by providing a plurality of electrodes capable of electrochemically detecting metabolic analytes in solution. Incorporation of this electrochemical measuring system of Hanagan into the apparatus of Kanegasaki would allow for a second means to determine cell behavior in addition to simple visual observation. Hanagan teaches that electrical detection using a patterned array of electrodes offers a rapid, automated and multiplexed analysis of cell culture analytes in real time.

Regarding Claims 4-7 and 52-55, the combination of Kanegasaki, Hanagan and Breznak disclose the bioreactor set forth in claims 1 and 49. The bioreactor disclosed by Kanegasaki is considered to be fully capable of accommodating any type of microorganism including bacteria, protozoa, tumor cells, endothelial cells, and normal tissue cells.

Regarding Claims 13, 15 and 61, Kanegasaki ('571) discloses the bioreactor set forth in claim 1 and 49 wherein at least one auxiliary port and channel are provided in fluid communication with the input and outlet ports. Kanegasaki teaches that additional ports (Figure

3:4Ba and Figure 3:4Aa) are used in conjunction with inlet (Figure 3:3Aa) and outlet (Figure 3:3Ba) ports, so as to supply extra reagents to the subchambers.

Regarding Claims 14, 16-17, 20, 22, 29-30, 39, 42-43, 48 and 75, with respect to the intended use limitations, the device disclosed by the combination of Kanegasaki, Hanagan and Breznak, is structurally the same as the instantly claimed and is capable of providing the operating conditions listed in the intended use section of the claim. Note statements of intended use carry no patentable weight when the structure of the Claim has been met by the prior art reference.

Regarding Claims 25, and 63, Kanegasaki ('571) discloses wherein the first substrate is formed from silicon (Paragraph 154).

Regarding Claims 44 and 71, Kanegasaki ('571) discloses a means positioned in the channel and adapted for monitoring of the cells therein (Paragraphs 163-164).

Claims 9-12 and 57-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Hanagan (US 5520787) and Breznak (US 5589352) as applied to claims 1 and 49, and further in view of Griffith et al. (US 6197575) or Thomas (US 20060194273).

Regarding Claims 9-12 and 57-60, the combination of Kanegasaki, Hanagan and Breznak disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose the use of cell adhesion coatings.

Griffith ('575) teaches that it is known in the art to modify surface properties by applying biocompatible coatings to the surfaces in order to promote cell adhesion or inhibit cell adhesion (Col 17, lines 28-39 and Col 18, lines 10-16).

At the time of the invention, it would have been obvious to utilize the surface modification disclosed by Griffith in the apparatus set forth by the combination of Kanegasaki, Hanagan and Breznak. In paragraph 160, Kanegasaki teaches that materials that encourage cell adhesion to substrate surfaces are beneficial. One of ordinary skill in the art would have recognized that the application of a coating to the substrate of Kanegasaki would have required only minor structural alterations, and would be completed in a predictable manner while yielding predictable results.

Thomas ('273) discloses the bioreactor as previously described above. In paragraphs [0040] and [0042], Thomas teaches that biocompatible coatings are applied to the surfaces of the cell chamber in order to promote cell adhesion.

Kanegasaki and Thomas are analogous art because they are from the same field of endeavor regarding microfluidic bioreactors.

At the time of the invention, it would have been obvious to utilize the adhesion promoting coatings disclosed by Thomas in the apparatus set forth by Kanegasaki. In paragraph [0160], Kanegasaki teaches that materials that encourage cell adhesion to substrate surfaces are beneficial. One of ordinary skill in the art would have recognized that the application of a coating to the substrate of Kanegasaki would have required only minor structural alterations, and would be completed in a predictable manner while yielding predictable results.

Claims 19 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Hanagan (US 5520787) and Breznak (US 5589352) as applied above to claims 1 and 49, further in view of Sparks (US 5157438).

Regarding Claims 19 and 24, Kanegasaki ('571) discloses a cover cap (Figure 39:17) but does not expressly disclose wherein the cover cap is adapted for slidably covering or opening the open end of the sample chamber.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Kanegasaki with a cover for slidably covering or opening the sample chamber since Sparks ('438) discloses that it was known in the art at the time the invention was made to provide a cover (lid) which can slidably engage covering or opening a sample chamber (Col 3, lines 1-7).

Claims 32 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Hanagan (US 5520787) and Breznak (US 5589352) as applied above to claims 31 and 69, further in view of Henkens et al. (US 6391558).

The combination of Kanegasaki Hanagan and Breznak do not disclose a multiplexed potentiostat.

Henkens et al. ('558) disclose an electrochemical detection device which comprises a multiplexed potentiostat (Col 5, lines 3-8).

It would have been obvious to one having ordinary kill in the art at the time the invention was made to modify the combination of Kanegasaki, and Lynes with a multiplexed potentiostat as taught by Henkens in order to measure the current of different targets.

Claims 33-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Hanagan (US 5520787) and Breznak (US 5589352) as applied above to claims 28, further in view of Quake (US 20020164816).

Regarding Claims 33-36, the combination of Kanegasaki Hanagan and Breznak does do not disclose a plurality of controlling ports comprising a fluid control valve.

Quake ('816) teaches that pumps and valves generally are designed to controls the movement and direction of fluids containing such materials within flow channels of the microfluidic devices. Generally, pump and valve systems employ pressure or other known actuation systems to affect fluid movement and direction in flow channels. Other fluid movement and direction controls for microfluidic devices are known in the art, including mechanical pumps and valves (Paragraph 206).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify Kanegasaki with a control port since Quake ('816) discloses that it was known in the art at the time the invention was made to provide fluid movement and direction controls.

Regarding Claims 37-39, it would have been obvious to one having ordinary skill in the art at the time the invention was made to position the counter electrode and working electrode between the fluid control valve and controlling port, since it has been held that rearranging parts of an invention involves only routine skill in the art. *In re Japikse,* 86 USPQ 70.

With respect to the intended use limitations, the device disclosed by the combination of Kanegasaki Hanagan and Breznak and Quake, is structurally the same as the instantly claimed and is capable of providing the operating conditions listed in the intended use section of the claim. Note statements of intended use carry no patentable weight when the structure of the Claim has been met by the prior art reference.

Claims 45-46 and 72-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Hanagan (US 5520787) and Breznak (US 5589352) as applied above to claims 44 and 71, further in view of Rao (US 20020025547) or Allen (US 20040142409).

Regarding Claims 45-46 and 72-73, the combination of Kanegasaki, Hanagan and Breznak disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection

above. Although Kanegasaki discloses in paragraphs [0163]-[0165] an optical system for the interrogation of motile cells, Kanegasaki does not indicate that the optical sensors and light sources are provided on a substrate above the first substrate.

Kanegasaki and Rao are analogous art because they are from the same field of endeavor regarding optical means for monitoring cell movement in a microfluidic system.

Rao ('547) discloses an optical chemical sensor which is excited by a light emitting diode wherein detection can occur via optical fibers coupled to a single diode array (Paragraphs 78-90).

At the time of the invention, it would have been obvious to provide the Kanegasaki device with an optical sensor, LED light sources and other optical detection means well known in the art. As evidenced by Rao, it is well known in the art to provide a bioreactor with an optical sensing system.

Allen discloses a detection system for monitoring the movement and presence of a cell (Figure 1:56) in a solution. An upper substrate (Figure 1:25) is provided above the base substrate (Figure 1:10), and serves to house a light source (Figure 1:30) and a photodetector (Figure 1:40). This is described in paragraphs [0033]-[0035].

Kanegasaki and Allen are analogous art because they are from the same field of endeavor regarding optical means for monitoring cell movement in a microfluidic system.

At the time of the invention, it would have been obvious to provide the Kanegasaki device with an additional substrate capable of holding a plurality of optical sensors, LED light sources and other optical detection means well known in the art. By arranging all critical optical components on an independent substrate, the overall apparatus would be characterized by a modular construction that would allow one to add and remove the optical devices with greater

ease. As evidenced by Allen, it is well known in the art to form important detection means integral with a substrate formed above a culture chamber.

Claims 47 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Hanagan (US 5520787) and Breznak (US 5589352) as applied above to claims 44 and 71, further in view of in view of Anderson et al. (US 6168948).

Regarding Claims 47 and 74 Kanegasaki does not disclose wherein the means for monitoring of the cells comprises at least one electrical sensor and at least one lead in electrical communication with a corresponding electrical sensor.

Anderson et al. ('948) discloses at least one electrical sensor and at least one lead in electrical communication with a corresponding electrical sensor (Col 43, line 65-Col 44, line 5).

At the time of the invention, it would have been obvious to provide the Kanegasaki device with an electrical sensor. As evidenced by Anderson, it is well known in the art to use an electrical sensor to monitor the various reactions.

Claim 76 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Herman et al (US 20010044143).

Regarding Claims 76, Kanegasaki ('571) discloses a bioreactor for cultivating cells in a liquid medium comprising a first substrate (Figure 5:7) having first and second surfaces defining a chamber therebetween. A barrier comprising a channel (Figure 5:1) and a plurality of protrusions (Figure 5:6) serve to divide the chamber into a first subchamber (Figure 5:2A) and a second subchamber (Figure 5:2B). This is disclosed in paragraphs [0084], [0085] and [0095]. Paragraph [0097] states that the protrusions and grooves formed within the channels are varied in order to control the diffusion of a particular cell type between the subchambers. Paragraph [121] states that the gaps of the barrier range from 3 to 50 microns. Figure 12 and paragraph [112] describe another configuration in which first and second barriers (1) are positioned so as to form

a central chamber (2A), an intermediate chamber (2B), and an outer chamber (2C). Furthermore, Kanegasaki teaches that an input port (Figure 3:3Aa) and an input transfer channel are formed in the substrate and provided in fluid communication with the first subchamber. Furthermore, an outlet port (Figure 3:3Ba) and an outlet transfer channel are provided in communication with the second subchamber. Kanegasaki does not disclose the use of biofilms.

Herman et al. ('143) disclose the use of biofilms in Paragraph 45.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Kanegasaki to include biofilms since Herman ('143) discloses that it was known in the art at the time the invention was made to provide biofilms.

Claim 77 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Herman et al (US 20010044143) as applied above to Claim 76, further in view of Turner et al. (US 5624537).

Regarding Claim 77, Kanegasaki does not disclose the use of a bolus of selected chemicals.

Turner et al. ('537) discloses the use of a bolus of chemicals (Col 18, line 61-61 and Col 19, lines 6-7).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Kanegasaki to include a bolus of chemicals and or reagents since Turner ('537) discloses that it was known in the art at the time the invention was made to provide a bolus of chemicals.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LYDIA EDWARDS whose telephone number is (571)270-3242. The examiner can normally be reached on Mon-Thur 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Walter Griffin can be reached on 571.272.1447. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LYDIA EDWARDS/
Examiner
Art Unit 1797

LE

/Walter D. Griffin/
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